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EXAMINER
RAWLINGS, STEPHEN L

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/964,275	DAI ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *1-6,9-13 and 17-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,8 and 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

1. The election filed September 15, 2003 is acknowledged and has been entered. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant has elected the invention of group XVI, claims 7, 8, and 14-16, insofar as the claims drawn to a nucleic acid molecule encoding a polypeptide comprising SEQ ID NO: 2, wherein said nucleic acid molecule consists of SEQ ID NO: 1, an expression vector comprising said nucleic acid molecule, a host cell comprising said vector, and a method for producing a polypeptide encoded by said nucleic acid molecule.

2. Claims 1-26 are pending in the application. Claims 1-6, 9-13, and 17-26 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

3. Claims 7, 8, and 14-16 are currently under prosecution.

Election/Restrictions

4. In the Response filed September 15, 2003, Applicant has requested non-elected claims be held in abeyance pending Applicant's decision as to whether to file a divisional application or applications directed to such claims. In reply, it is noted that the examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is

earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Sequence Rules Compliance

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be further examined under 35 U.S.C. §§ 131 and 132.

As noted on the attached Notice to Comply, sequence disclosures at page 5 in lines 25 and 26, which are of sufficient length to fall under the requirements set forth under 37 CFR §§ 1.821-1.825, are not properly identified by sequence identification numbers. As noted in the attached Notice to Comply, appropriate action correcting this deficiency is required.

Applicant is given the same period of time within which to reply to this Office action to comply with the sequence rules under 37 C.F.R. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g).

Specification

6. The specification is objected to because the use of numerous improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Examples of improperly demarcated trademarks include GenBank™ (page 9), Trans-Blot™ (page 17), Lambda Zap Express™ (page 18), Exassist™ (pages 18 and 19), and Qiagen™ (page 19).

Appropriate corrections are required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

7. The abstract of the disclosure is objected to because the abstract should be a single paragraph. Correction is required. See MPEP § 608.01(b).

8. The specification is objected to because of the following informality: At page 9, line 21, the reference reads, "nat Genet.", where it should read, "Nat Genet." Correction is required.

Response to Amendment

9. The amendment filed October 11, 2001 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material, which is not supported by the original disclosure, is: "and incorporates the same by reference", wherein the "same" is reference to copending application number "U 013652-6", i.e., US Application No. 09/961,803, filed September 24, 2001. An incorporation-by-reference statement added after the filing date of an application is not permitted because no new matter can be added to an application after its filing date. See 35 U.S.C. § 132(a). When a benefit claim is submitted after the filing of an application, the reference to the prior application cannot include an incorporation-by-reference statement of the prior application. Therefore, the incorporation-by-reference statement in the amendment to the specification introduces new matter and renders the amendment improper. See *Dart Industries v. Banner*, 636 F.2d 684, 207 USPQ 273 (C.A.D.C. 1980). See 1268 OG 89 (18 March 2003).

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

10. Claims 7, 8, and 14-16 are objected to because of the following informalities:

(a) Claims 7, 8, and 14-16 are drawn in the alternative to the subject matter of non-elected inventions. Appropriate correction is required.

(b) Claims 7, 8, and 14-16 depend upon non-elected claims. Appropriate correction is required.

Claim Rejections - 35 USC § 101

11. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

12. Claim 15 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 15 is drawn to a host cell comprising the vector of claim 14.

At page 6, lines 15-19, the specification defines "host cell" without apparent limitation. Therefore, the claim is broadly interpreted to encompass host cells, which are not isolated and are comprised within an organism. Thus, the claim encompasses host cells that have been transfected with the vector of claim 14 that are comprised within a transgenic animal, including a human.

MPEP § 2105 [R-1] states:

> If the broadest reasonable interpretation of the claimed invention as a whole encompasses a human being, then a rejection under 35 U.S.C. 101 must be made indicating that the claimed invention is directed to nonstatutory subject matter.

Amending claim 15 to recite "isolated" before "host cell" can obviate this ground of rejection.

13. Claims 7, 8, and 14-16 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

The instant application provides a description of a polynucleotide sequence encoding a protein. The protein, which has the predicted amino acid sequence set forth in SEQ ID NO: 2, is what is termed in the art, an "orphan protein". This is a protein that is encoded by a complementary DNA (cDNA) molecule, which has been isolated by virtue of its having a polynucleotide sequence having similarity to other known cDNA molecules. The observed similarity between the polynucleotide sequences, or the amino acid sequences encoded thereby often leads to speculation that the protein will be found to have a particular function. In this instance, the polynucleotide sequence encoding SEQ ID NO: 2 is similar to the polynucleotide sequence encoding NOC-2.

Indeed, it is not unlikely that after further characterization the protein of SEQ ID NO: 2, which is putatively encoded by the claimed nucleic acid molecule comprising SEQ ID NO: 1, will be found to have a specific utility. However, until the further characterization of the protein encoded by the newly discovered polynucleotide sequence has been completed establishing the protein's putative function, the polynucleotide sequence is only a novelty, and the claimed invention is therefore not a finished invention having an established utility.

The instant situation is directly analogous to that which was addressed in *Brenner, Comr. Pats. v. Manson,* 148 U.S.P.Q. 689 (US SupCt, 1966). A novel compound, which was found to be structurally analogous to other compounds known to possess anti-cancer activity, was alleged to be useful by virtue of its structural similarity to these other useful compounds but otherwise, in the absence of factual evidence. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The Court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. Id., at 695.

Further, the Court opined,

> [W]e are [not] blind to the prospect that what now seems without "use" may tomorrow command the grateful attention of the public. But a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. Id., at 696.

Accordingly, as the instant claims are drawn to a nucleic acid molecule encoding a polypeptide of, as yet, an undetermined function or biological significance, until some actual and specific significance can be attributed to the polypeptide of SEQ ID NO: 2, or *NL1,* as it is named in the disclosure, the inventive process has not been refined or developed to a point where a specific benefit can be derived by the public from the

granting of a patent upon the Applicant's application. Moreover, in the absence of any established functional or biological significance, there is no immediately obvious "patentable" use for the claimed invention; nor does the specification assert the claimed invention can be used by the skilled artisan in any manner specific to the chemical and biologic nature of the nucleic acid molecule, or the protein encoded thereby, which might provide an immediate benefit to the public. Because the specification does not disclose a currently available, "real world" use for the claimed antibody, the requirements set forth under 35 U.S.C. § 101 have not been met.

The existing information disclosed by Applicant's application would merely provide the artisan with an invitation to perform such investigations, which might ultimately lead to a derivation of a specific benefit, or which might not; and in either case, an immediate benefit could not be derived from the use of the claimed invention because the existing information is insufficient to enable the artisan to use the claimed polynucleotide in the manner asserted to provide an immediate benefit. Although the disclosure of the claimed polynucleotide might tomorrow command the grateful attention of the public, the Court has decided:

> [A] patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.

Brenner, Comr. Pats. v. Manson, 148 U.S.P.Q. 689 at 696 (US SupCt, 1966).

The generic usefulness of a nucleic acid molecule is not disputed, as any nucleic acid molecule can be used, for example, as the specification asserts, as a probe to monitor gene expression or to produce a protein encoded thereby. However, because an nucleic acid molecule is generically useful as a such a reagent, the assertion that the claimed invention can be used as in such a manner lacks specificity. Similarly, while the specification discloses the protein encoded by the claimed nucleic acid molecule can be used as an immunogen to produce an antibody that binds the protein, any protein can be used in this manner; again, the asserted utility is not specific to the structure and nature of the disclosed invention. Therefore, any benefit that might be derived by the public for a grant of a patent monopoly of the existing information disclosed by Applicant's application is not specific to the substance and nature of the

claimed antibody. See *Brenner, Comr Pats v. Manson*, 148 USPQ 689 (US SupCt, 1966).

Applicants have asserted that other disclosed nucleic acid molecules, which were isolated from cDNA libraries derived from cancer cells, might have specific utility, but the claimed invention was isolated from a cDNA library derived from normal lung cells. Moreover, Applicant has not shown that the expression, or absence thereof, or the activity, or lack thereof, of the polypeptide encoded by the claimed nucleic acid molecule is associated with any particular disease or disorder. In fact, Applicant has not described the function of the protein encoded by the claimed nucleic acid molecule.

Although it does not appear that Applicant has asserted the claimed invention has any particular and specific utility, it is aptly noted that any utility the invention might be presumed to have would necessarily be founded upon a presumption that the protein to which the antibody must bind will have activity similar to NOC2, or will be associated with the etiology or pathology of cancer. Such presumption would be entirely based upon database searches and sequence comparisons alone. Yet, the skilled artisan cannot predict whether a protein will have a particular activity simply because the protein is homologous to another protein known to have such an activity. Furthermore, the skilled artisan cannot predict whether a given polypeptide is associated with etiology or pathology of cancer, simply because the amino acid sequence of the protein is similar to the amino acid sequence of another protein known to have such an association. Bowie et al. (*Science* 1990; **257**: 1306-1310) teaches that an amino acid sequence encodes a message that determines the shape and function of a protein; and, that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome. Bowie et al. also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (page 1306, column 1). Bowie et al. teaches that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the

sequence are critical to the three-dimensional structure/function relationship and these regions can tolerate only conservative substitutions or none at all (page 1306, column 2). Burgess et al. (*Journal of Cell Biology* 1990; **111**: 2129-2138) teaches the sensitivity of proteins to alterations of even a single amino acid in a sequence. This reference teaches that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Lazar et al. (*Molecular and Cellular Biology* 1988; **8**: 1247-1252) teaches that a replacement of aspartic acid at position 47 with alanine or asparagine in transforming growth factor alpha had no effect but that a replacement with serine or glutamic acid sharply reduced its biological activity. The disclosures of Burgess et al. and Lazar et al. teach that even a single amino acid substitution can often dramatically affect the biological activity and the structure-function characteristics of a protein. Yet, at page 9, for example, the specification discloses the claimed nucleic acid molecule encodes a protein that differs substantially from NOC2; and therefore one skilled in the art would not expect the function of the polypeptide encoded by the claimed nucleic acid molecule to be the same as that of NOC2. Skolnick et al. (*Trends in Biotechnology* 2000; **18**: 34-39) discloses that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (see, e.g., the abstract; and page 34, *Sequence-based approaches to function prediction*). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see, in particular, the abstract and Box 2). Thus, the function of a polypeptide cannot be predicted upon the basis of an observed sequence similarity to another protein; nor can the function of a polypeptide be reasonably inferred by a disclosed homology to another protein.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 7, 8, and 14-16 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

16. If the above rejection of claims 7, 8, and 14-16 under 35 USC § 101 were to be overcome, claim 15 would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using an isolated host cell comprising the vector of claim 14, does not reasonably provide enablement for any host cell comprising the vector of claim 14. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 15 is drawn to a host cell comprising the vector of claim 14. At page 6, lines 15-19, the specification defines "host cell" without apparent limitation. Therefore, the claim is broadly interpreted to encompass host cells, which are not isolated and are comprised within an organism. Thus, the claims encompass host cells that have been transfected with the vector of claims 5 or 6 that are comprised within a transgenic animal, including nonhuman or human animals and animals treated using gene therapy.

Support for this interpretation of the claims can be found in the specification at pages page 12, lines 8-16, and page 17, lines 4 and 5.

The teachings of the specification cannot be extrapolated to the enablement of the claimed invention because the amount of guidance, direction, and exemplification set forth therein would not be sufficient to enable the skilled artisan to have a reasonable expectation of success in making and using the claimed invention without the need to perform additional, and an undue amount of experimentation. Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). These factors include the nature of

the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The specification does not provide a sufficient amount of guidance, direction, or exemplification to enable the skilled artisan to make or use host cells that are comprised within a non-human transgenic animal. In the art of producing transgenic animals, the phenotype of the resultant transgenic animal is not always predicable or viable. Houdebine (*Journal of Biotechnology* 1994, 34: 269-287) teaches the vectors to be used for directing the expression of transgenes in any given tissue, or in all tissues, must contain the appropriate regulatory regions. Houdebine teaches expression is heavily dependent on the site of integration in the host genome and the site of integration is presently unpredictable. Therefore, it is concluded that one of skill in the art would need to perform undue experimentation in order to make and use the claimed host comprised within a transgenic animal.

In addition, the specification does not teach provide a sufficient amount of guidance, direction, and exemplification to enable the skilled artisan to have a reasonable expectation of successfully producing host cells within a living organism, which comprise the vectors of claim 14, by gene transfer, or *gene therapy*. The art of gene therapy, i.e., the *in vivo* delivery genetic information to targeted cells within a body using naked DNA or viral vectors or by reintroducing *ex vivo* modified host cells into the body, is still in its infancy. Moreover, the art is highly unpredictable and its successful application has been hindered by numerous limitations, which the specification does not remedy and would preclude the skilled artisan from having a reasonable expectation of successfully making and using the claimed invention without need of performing an undue amount of experimentation.

For example, the teachings of the specification have not overcome the problems with *in vivo* delivery and expression. Verma et al. (*Nature* 1997, **389**: 239-242) teach that the Achilles heel of gene therapy is gene delivery. Verma et al. state that the

ongoing problem is the inability to deliver genes efficiently and to obtain sustained expression. Similarly, Amalfitano et al. (*Current Gene Therapy* 2002, **2**: 111-133) teach that non-viral mediated transfer of DNA generally suffers from low transduction efficiencies. In addition, Amalfitano et al. discuss numerous limitations that have been encountered in using retroviral vectors to deliver DNA into a subject and teach the use of adenoviral vectors can be ineffective because of the induction of strong immune responses in the host to the viral vectors and direct acute and chronic toxicity caused by the vector itself.

It is noted that Amalfitano et al. teach that a despite general lack of success, the first conclusive evidence that gene therapy can show efficacy in humans was achieved in human X-linked SCID subjects *via* retrovirus transduction. However, since the publication, The Department of Health and Human Services has released a memorandum dated January 14, 2003, a copy of which is attached to this Office action, that urges all such investigations to be discontinued until new data are available, the possible etiology and risks of adverse events associated are considered, and recommendations emerge. Despite the initial promise of the trial studying gene transfer as a possible treatment for the disease, investigators have found that retroviral-mediated insertion of the transgene has caused the subjects to develop cancer. The results of the trial underscore the high degree of unpredictability associated with the art and the fact that the skilled artisan could not make or use the claimed invention with a reasonable expectation of success without need to perform additional experimentation.

The state of the art, as a whole, is well defined by Pandha et al. (*Current Opinion in Investigational Drugs* 2000; **1** (1): 122-134) in the abstract. Pandha et al. teach:

> Despite the rapid technological advances that continue to sustain the field of cancer gene therapy, few individual patients have benefited from the revolution so far. The plethora of clinical trials described confirms that each malignancy will have its own ideal strategy based on the associated molecular defects, and there has been rapid progress from this viewpoint. At the same time, there has been a renewed appreciation for the limitations to gene therapy, which include low efficiency of gene transfer, poor specificity of response and methods to accurately evaluate responses, and lack of truly tumor-specific targets at which to aim. As with all new therapies, we are climbing a steep learning curve in terms of encountering treatment-related toxicities, as well as profound ethical and regulatory issues.

In view of the preponderance of evidence establishing the state of the art, now and at the time the application was filed, and the level of unpredictability associated therewith, in the absence of a disclosure of an amount of guidance, direction, and exemplification that is reasonably commensurate in scope with the claims, it appears that skilled artisan could not make and use the claimed invention with a reasonable expectation of success without having the need to perform an undue amount of experimentation.

Amending claim 15 to recite "isolated" before "host cell" can obviate these grounds of rejection.

Conclusion

17. No claims are allowed.

18. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. Kotake et al., Haynes et al., and Fukada teach Noc2.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne (Bonnie) Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
March 15, 2004